

What is claimed is:

- Sub. 017*
1. An isolated polynucleotide selected from the group consisting of:
 - (a) SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13 or SEQ ID NO:15;
 - (b) the sequence of (a), wherein T can also be U;
 - (c) nucleic acid sequences complementary to the sequence of a); and
 - (d) fragments of (a), (b), or (c) that are at least 15 bases in length and that will hybridize under moderate to highly stringent conditions to DNA that encodes the Phospholipid Scramblase protein of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:14 or SEQ ID NO:16, respectively.
 2. An expression vector containing a polynucleotide of claim 1.
 3. The vector of claim 2, wherein the vector is a plasmid.
 4. The vector of claim 2, wherein the vector is a viral vector.
 5. A host cell containing a vector of claim 2.
 6. The host cell of claim 5, wherein the cell is prokaryotic.
 7. The host cell of claim 5, wherein the cell is eukaryotic.
 8. A substantially purified Phospholipid Scramblase polypeptide, wherein the polypeptide is encoded by polynucleotide as set forth in SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:13 or SEQ ID NO:15.
 9. A substantially purified Phospholipid Scramblase polypeptide, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:14 or SEQ ID NO:16, or fragments thereof.

10. Antibodies which bind to a polypeptide of claim 8, or fragments thereof.
11. The antibodies of claim 10, wherein the antibodies are polyclonal.
12. The antibodies of claim 10, wherein the antibodies are monoclonal.
13. A method for producing a polypeptide comprising an amino acid sequence of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:14 or SEQ ID NO:16, the method comprising:
 - (a) culturing a host cell of claim 5 under conditions suitable for the expression of the polypeptide; and
 - (b) recovering the polypeptide from the host cell culture.
14. An isolated nucleic acid sequence comprising a non-coding regulatory sequence isolated upstream from a Phospholipid Scramblase gene, wherein the nucleic acid sequence contains at least one restriction site for cloning a heterologous nucleic acid sequence of interest.
15. The isolated nucleic acid sequence of claim 14, wherein the sequence is operably linked to a heterologous nucleic acid sequence thereby forming a DNA construct.
16. The isolated nucleic acid sequence of claim 14 wherein the heterologous nucleic acid sequence is selected from the group consisting of a nucleic acid sequence encoding a selectable marker gene, the glucuronidase (GUS) reporter gene, and the luciferase (LUC) reporter gene.

17. A method of identifying a compound that modulates expression of a Phospholipid Scramblase polypeptide, wherein the method comprises;
 - (a) incubating the compound with a cell containing the DNA construct of claim 15 under conditions sufficient to permit the compound to interact with the construct;
 - (b) detecting expression of the heterologous gene in the presence of the compound wherein an increase or decrease in the expression of the heterologous gene in the presence of the compound compared to expression in the absence of the compound identifies compounds that modulate Phospholipid Scramblase polypeptide expression.
18. The method of claim 17, wherein the modulation is inhibition of Phospholipid Scramblase expression.
19. The method of claim 17, wherein the modulation is stimulation of Phospholipid Scramblase expression.
20. The method of claim 17, wherein the compound is selected from the group consisting of peptides, peptidomimetics, polypeptides, pharmaceuticals, chemical compounds, biological agents, antibodies and trophic agents.
21. A transgenic knockout mouse whose genome comprises a disruption of a Phospholipid Scramblase polypeptide gene, wherein said disruption comprises the insertion of a transgene comprising a selectable marker sequence, and wherein said disruption results in the mouse exhibiting a higher susceptibility to viral infection or cancer as compared to a wild-type mouse.
22. The transgenic knockout mouse of claim 21, wherein the mouse is homozygous or heterozygous for said disruption of the endogenous Phospholipid Scramblase polypeptide gene.

23. The transgenic knockout mouse of claim 22, wherein the endogenous Phospholipid Scramblase polypeptide gene contains the polynucleotide sequence as set forth in SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13 or SEQ ID NO:15.
24. A method for producing a transgenic mouse exhibiting an increased susceptibility to viral infection or to cancer, said method comprising:
- (a) introducing a transgene comprising a selectable marker sequence into a mouse embryonic stem cell;
 - (b) introducing the mouse embryonic stem cell into a mouse embryo;
 - (c) transplanting the embryo into a pseudopregnant mouse;
 - (d) allowing the embryo to develop to term; and
 - (e) identifying a transgenic mouse whose genome comprises a disruption of the endogenous Phospholipid Scramblase polypeptide gene, wherein the disruption results in the mouse exhibiting an increased susceptibility to viral infection or to cancer as compared to a wild-type mouse.
25. The method of claim 24, wherein the transgenic mouse is homozygous or heterozygous for the disruption of the endogenous Phospholipid Scramblase polypeptide gene.
26. A method of inhibiting or preventing viral infection comprising introducing into viral-infected cells or uninfected cells a Phospholipid Scramblase polypeptide or fragments thereof containing the amino acid sequence PPxY.
27. The method of claim 26, wherein the viral infection is an infection of a virus selected from the group consisting of a rhabdovirus, a filovirus, a retrovirus, a flavivirus, a coronavirus, a orthomyxovirus, a bunyavirus, a hepadnavirus, a herpesvirus, a poxvirus, a togavirus, a iridovirus, a paramyxovirus and a arenavirus.

28. The method of claim 27, wherein the viral infection is selected from the group consisting of an HIV infection, an Ebola virus infection, a Marburg virus infection and a Rabies virus infection.

29. The method of claim 26, wherein the virus infection is an infection of a membrane-bound virus.

30. The method of claim 26, wherein the polypeptides and fragments bind to proteins containing one or more WW domain sequence motifs.

31. The method of claim 26, wherein the Phospholipid Scramblase polypeptide is interferon-inducible.

32. The method of claim 31, wherein the Phospholipid Scramblase polypeptide has the amino acid sequence as set forth in SEQ ID NO:2.

33. The method of claim 26, further comprising administering an interferon.

~~34. The method of claim 26 wherein the fragments are peptidomimetics.~~

35. A method for identifying a compound that modulates Phospholipid Scramblase polypeptide activity:

- (a) incubating the compound with a cell expressing a Phospholipid Scramblase polypeptide under conditions sufficient to permit the compound to interact with the cell;
- (b) comparing the cellular response in a cell incubated with the compound with the cellular response of a cell not incubated with the compound, thereby identifying a compound that modulates Phospholipid Scramblase polypeptide activity.

36. The method of claim 35, wherein the cellular response is a decrease in Phospholipid Scramblase polypeptide activity.
37. The method of claim 35, wherein the cellular response is an increase in Phospholipid Scramblase polypeptide activity.
38. A method of treating a disorder associated with Phospholipid Scramblase polypeptide activity comprising administering to a subject in need thereof a therapeutically effective amount of a compound that modulates a Phospholipid Scramblase polypeptide activity.
39. The method of claim 38, wherein the disorder is a viral infection or a cancer.
40. The method of claim 38, wherein the viral infection is an infection of a rhabdovirus, a filovirus, a retrovirus, a flavivirus, a coronavirus, a orthomyxovirus, a bunyavirus, a hepadnavirus, a herpesvirus, a poxvirus, a togavirus, a iridovirus, a paramyxovirus or a arenavirus, an infection of a rhabdovirus, a filovirus or a retrovirus.
41. The method of claim 40, wherein the viral infection is an HIV infection, an Ebola virus infection, a Marburg virus infection or a Rabies virus infection.
42. The method of claim 39, wherein the cancer is hairy cell leukemia, chronic myelogenous leukemia, myeloma, melanoma, renal cell carcinoma, Kaposi's sarcoma, follicular lymphoma, thrombocythemia or erythroleukemia.
43. The method of claim 38, wherein the compound comprises an agonist or antagonist of a Phospholipid Scramblase polypeptide activity.
44. The method of claim 38, wherein the compound is selected from the group consisting of peptides, peptidomimetics, polypeptides, pharmaceuticals, chemical compounds, biological agents, antibodies and trophic agents.

45. The method of claim 38, wherein the Phospholipid Scramblase polypeptide activity is activity of a polypeptide as set forth in SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8.
46. The method of claim 45, wherein the Phospholipid Scramblase polypeptide is interferon-inducible.
47. The method of claim 46, wherein the Phospholipid Scramblase polypeptide has the amino acid sequence as set forth in SEQ ID NO:2.
48. The method of claim 38, further comprising administering an interferon.
49. A method of diagnosis of a subject having or at risk of having a Phospholipid Scramblase-related disorder comprising detecting in the subject a level or activity of a Phospholipid Scramblase polypeptide wherein a difference in the level or activity of a Phospholipid Scramblase polypeptide in the subject from a level or activity of a Phospholipid Scramblase polypeptide in a normal subject is indicative of a Phospholipid Scramblase-related disorder.
50. The method of claim 49, wherein the Phospholipid Scramblase-related disorder is cancer or virus infection.
51. The method of claim 50, wherein the cancer is hairy cell leukemia, chronic myelogenous leukemia, myeloma, melanoma, renal cell carcinoma, Kaposi's sarcoma, follicular lymphoma, thrombocythemia or erythroleukemia.
52. The method of claim 50, wherein the virus infection is an infection of a rhabdovirus, a filovirus, a retrovirus, a flavivirus, a coronavirus, a orthomyxovirus, a bunyavirus, a hepadnavirus, a herpesvirus, a poxvirus, a togavirus, a iridovirus, a paramyxovirus or a arenavirus, an infection of a rhabdovirus, a filovirus or a retrovirus.
53. The method of claim 52, wherein the virus infection is an HIV infection, an Ebola virus infection, a Marburg virus infection or a Rabies virus infection.

54. The method according to claim 49, wherein the level or activity of a Phospholipid Scramblase polypeptide in the subject having or at risk of having Phospholipid Scramblase-related disorder is lower than the level of a of Phospholipid Scramblase polypeptide in a normal subject.
55. A method of increasing or extending the viability of mammalian cells or tissues by inhibiting the expression of a Phospholipid Scramblase polynucleotide within the cell or tissue.
56. The method according to claim 55, wherein the polynucleotide is selected from:
- (a) SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13 or SEQ ID NO:15
 - (b) the sequence of (a), wherein T can also be U;
 - (c) nucleic acid sequences complementary to the sequence of (a); and
 - (d) fragments of (a), (b), or (c) that are at least 15 bases in length and that will hybridize under moderate to highly stringent conditions to DNA that encodes the Phospholipid Scramblase protein of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14 or SEQ ID NO:16, respectively.
57. The method according to claim 55, wherein the polynucleotide is selected from the group consisting of SEQ ID NO:1; SEQ ID NO:1, where T can also be U; nucleic acid sequences complementary thereto; and fragments thereof that are at least 15 bases in length and that will hybridize under moderate to highly stringent conditions to DNA that encodes the Phospholipid Scramblase protein of SEQ ID NO:2.
58. A method of treating a subject having or at risk of having a disorder associated with a Phospholipid Scramblase polypeptide or polynucleotide comprising:
- introducing into a subject having or at risk of having the disorder a polynucleotide encoding the Phospholipid Scramblase polypeptide operatively linked to a regulatory sequence, thereby treating the subject.

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